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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,761	05/25/2006	Curtis Dobson	81599-3	7370

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,761	DOBSON, CURTIS	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March, 2009*, is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 26 March, 2009. Claims 1, 4-16, and 18-22 are pending in the instant application. Claims 18-22 stand withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (refer to 37 C.F.R. § 1.144 and M.P.E.P. § 821.01).

37 C.F.R. § 1.821-1.825

Acknowledgement is hereby made of receipt and entry of the sequence listing filed 26 March, 2009. The application is now in compliance with the sequence requirements.

37 C.F.R. § 1.84

Acknowledgement is hereby made of receipt and entry of the drawings filed on 26 March, 2009, which are deemed to be acceptable.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 1 and 4-16 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn in response to applicant's amendment.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

Claims 1 and 4-16 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The amended claims are directed toward antiviral polypeptides comprising $apoE_{141-149}$ tandem repeats, derivatives thereof, or truncations thereof. The parent tandem polypeptide has the amino acid sequence LRKLRKKRLLLRKLRKKRLL (SEQ ID No.: 2). It was also stipulated that said polypeptides carry at least one additional mutation (either W, K, or R) at one of the leucine residues in this polypeptide. It appears that only polypeptides having the recited mutations (either W, K, or R) in the L residues have the desired activity. Appropriately drafted claim language directed

toward these embodiments would be acceptable (e.g., **Claim 1. An isolated and purified antiviral polypeptide comprising between 14 and 18 amino acids of the apoE$_{141-149}$ tandem repeat set forth in SEQ ID NO.: 2, wherein said polypeptide comprises one or more amino acid substitutions of tryptophan (W) for leucine (L).**).

As previously set forth, the legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the maximum sequence lengths that result in retention of antiviral activity. The apoE$_{141-149}$ tandem repeat polypeptide is 18 amino acids in length. However, the claims do not recite any maximum sequence lengths. The skilled artisan would reasonably conclude that this polypeptide might not work when placed in the context of a much larger polypeptide (e.g., 25kDa, 50kDa, 100kDa, etc.) because of steric hindrance and other structural considerations.

2) The disclosure fails to provide adequate guidance pertaining to acceptable amino acid substitutions, additions, deletions, or modifications that will result in retention of antiviral activity. The amended claims are still directed toward derivatives of the parent $apoE_{141-149}$ tandem repeat polypeptide. The term derivative does not limit the polypeptide to any particular amino acid addition, deletion, or substitution. The claims do not limit mutations to any particular location in the polypeptide. The only minimal structural requirement dictates that at least one L:W substitution is present. Any of the remaining amino acids may contain additional replacements or deletions. The disclosure appears to suggest that substitutions of only three amino acid residues (K, R, and W) at existing L in the parent polypeptide display the requisite activity. Peptides having other amino acids substitutions at the Leu residues were not functional as were peptides having amino acid substitutions outside of these residues (see pp. 30, 32, and 35). This suggests the antiviral activity of the polypeptide requires a critical conformation that is not tolerant to single or multiple amino acid changes.

3) The claims encompass an inordinate number of polypeptide variants with single or multiple amino acid additions, deletions, and/or substitutions. However, the disclosure fails to provide adequate guidance pertaining to those regions that modulate antiviral activity.

4) The state-of-the-art as it pertains to antiviral development is replete with scientific obstacles. The generation of efficacious antivirals has proved difficult because of several factors including the quasispecies nature of many viral infections which leads to rapid drug resistance, the failure of

many compounds to display a favorable pharmacological profile, and the failure of many animal models to accurately predict clinical efficacy (Gait and Karn, 1995; Hirsch *et al.*, 1998).

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention in a manner commensurate in scope with the claims.

Response to Arguments

Applicants submit the proposed claim amendments provide a minimum/maximum sizes for the claimed polypeptides and suitable amino acid replacements, thereby obviating the rejection. This argument is not deemed to be persuasive for the reasons of record set forth *supra*. First, the claims are directed toward a polypeptide "comprising" the recited $apoE_{141-149}$ tandem repeat core polypeptide. Thus, the claim fails to impart any maximum sequence length. The only stipulation is that the peptide of interest comprise at least this core sequence. It has been well-documented in the prior art that adjacent, as well as, distal sequences can influence, often in a negative manner, the activities of a small polypeptide core sequence. Representative examples of larger polypeptides carrying the desired core sequence with the requisite activity were not provided. Second, the claims still recite polypeptide "derivatives". The skilled artisan would reasonably interpret this term to encompass additional amino acid additions, substitutions, or deletions, in addition to the specified L:W substitution. As noted in the rejection the specification suggests that these polypeptides fails to retain their antiviral activity if substitutions other than L:W are provided. Accordingly, the rejection is proper and

maintained. Applicant may obviate the rejection by adopting the claim language suggested *supra*.

Action Is Final

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c)

mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

08 June, 2009